UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/787,335	06/13/2001	Hermann-Joseph Grone	P/717-189	9473

1444 7590 03/18/2003

BROWDY AND NEIMARK, P.L.L.C.
624 NINTH STREET, NW
SUITE 300
WASHINGTON, DC 20001-5303

EXAMINER	
HAMUD, FOZIA M	

ART UNIT	PAPER NUMBER
1647	16

DATE MAILED: 03/18/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/787,335	Applicant(s) Grone et al.
	Examiner Fozia Hamud	Art Unit 1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) [X] Responsive to communication(s) filed on *Feb 21, 2003* .

2a) [ ] This action is **FINAL**. 2b) [X] This action is non-final.

3) [ ] Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) [X] Claim(s) *17-22, 24-33, and 35-37* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) [ ] Claim(s) _____ is/are allowed.

6) [X] Claim(s) *17-22, 24-33, and 35-37* is/are rejected.

7) [ ] Claim(s) _____ is/are objected to.

8) [ ] Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) [ ] The specification is objected to by the Examiner.

10) [ ] The drawing(s) filed on _____ is/are a) [ ] accepted or b) [ ] objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) [ ] The proposed drawing correction filed on _____ is: a) [ ] approved b) [ ] disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) [ ] The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) [ ] Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) [ ] All b) [ ] Some* c) [ ] None of:

1. [ ] Certified copies of the priority documents have been received.
2. [ ] Certified copies of the priority documents have been received in Application No. _____ .
3. [ ] Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) [ ] Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) [ ] The translation of the foreign language provisional application has been received.

15) [ ] Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) [ ] Notice of References Cited (PTO-892)
2) [ ] Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) [ ] Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) [ ] Interview Summary (PTO-413) Paper No(s). _____
5) [ ] Notice of Informal Patent Application (PTO-152)
6) [ ] Other:

DETAILED ACTION

1. Applicant's after final amendment filed on 21 February 2003 in Paper No.15 has been entered. Claims 17, 20, 27, 30 and 37 have been amended. Claims 17-22, 24-33, 35-37 are pending and are under consideration by the Examiner.

2. Upon reconsideration, the prosecution on the merits of this application is reopened and the finality of the rejection of the previous office action is withdrawn. Also the indicated allowability of claims 21-22 and 32-33 is withdrawn. The delay of the rejection of the claims is regretted.

Claim Rejections - 35 U.S.C. § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3a. Claims 17-22, 24-27, 29-33, 35-37, are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating or preventing the rejection of transplanted organs, tissues or cells in a mammal by administering a pharmaceutical composition comprising Met-RANTES in combination with low dose of Cyclosporin, and a pharmaceutical composition comprising Met-RANTES and said low dose Cyclosporin, does not reasonably provide enablement for a method of treating or preventing the rejection of transplanted organs tissues or cells in "all" possible subjects, by administering a pharmaceutical composition comprising "all possible" antagonists for all RANTES receptor and "all" possible dosages of Cyclosporin or a pharmaceutical composition comprising "all possible" antagonists for RANTES receptor and "all" possible dosages

of Cyclosporin, or wherein a RANTES receptor antagonist that is amino-terminally truncated or amino terminally extended. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 17 and 30 recite "a method of treating or preventing the rejection of transplanted organs, tissues or cells by administering a RANTES receptor antagonist in combination with a Cyclosporin ....." and "a pharmaceutical composition comprising ... a combination of a RANTES receptor antagonist and a Cyclosporin ", respectively, what is claimed in the instant invention broadly encompasses pharmaceutical compositions comprising "all" antagonists for RANTES receptor in combination with any dose of Cyclosporin and a method of using said pharmaceutical composition for treating or preventing the rejection of transplanted organs, tissues or cells in all possible subjects. While the specification discloses that Met-RANTES in combination with *low dose* of Cyclosporin caused significant reduction of interstitial rejection of renal allograft transplantation, significant reduction in the vascular and tubular damage and significant reduction in mononuclear cell infiltration, (see page 4, lines 16-27, page 16, lines 11-27 and table 2 and 3). Thus the only RANTES receptor antagonist that is disclosed in the instant method is Met-RANTES which is used in combination with low dose Cyclosporin for the treatment and prevention of the rejection of transplanted kidney. Therefore, the specification is non-enabling for the unlimited number RANTES receptor antagonists (amino-terminally truncated or extended) which are encompassed by the scope of the claims to be used in combination with Cyclosporin, because the claimed invention encompasses RANTES receptor antagonists not envisioned or described in the

specification, and neither does the specification disclose whether these claimed RANTES receptor antagonists in combination with Cyclosporin would have beneficial or detrimental effects on organ transplant patients. The specification discloses that adding a single methionine at the N-terminus of RANTES changes the agonist protein into a RANTES receptor antagonist with nonmolar potency, and that treatment of rat renal transplant model with Met-RANTES in combination with low dose of Cyclosporin caused a significant reduction of interstitial rejection in renal allograft transplantation, (page 16). Thus the only amino-terminally extended RANTES receptor antagonist to be used in combination with Cyclosporin, disclosed by Applicants is Met-RANTES. The specification describes the specific RANTES receptor antagonist Met-RANTES which has specific characteristics and properties. These properties differ structurally, chemically and physically from other known or unknown RANTES receptor antagonists. The criteria set forth in Ex parte Forman (230 USPQ 546 (Bd. Pat. App. & Int. 1986), and reiterated in In re Wands (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)), which include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims, is the basis for determining undue extermination. In the instant application, the only RANTES receptor antagonist disclosed and used in combination with Cyclosporin for the treatment and prevention of renal transplant rejection is Met-RANTES, and the skilled artisan would not be able to predict if other RANTES receptor antagonists in combination with Cyclosporin would have any significant effect on organ transplant rejection, whether they would have beneficial or detrimental effects on said

patients. There is no guidance that "all" RANTES receptor antagonists would function the way Met-RANTES did, neither does the specification provide any guidance of how many amino acids to delete from the N-terminus or how many amino acids to add to the N-terminus of RANTES.

Applicants show that Met-RANTES reduces the effective dose of Cyclosporin and that this unexpectedly reduces nephrotoxicity of Cyclosporin, (see page 6, lines 17-21). Thus, Applicants are only enabled for a method of treating or preventing the rejection of transplanted organs, tissues or cells in a mammal by administering a pharmaceutical composition comprising the RANTES receptor antagonist Met-RANTES in combination with *low dose* of Cyclosporin and a pharmaceutical composition comprising Met-RANTES and Cyclosporin.

3b. Claims 17-22, 24-27, 29-33, 35-37 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The written description in this case only discloses a method of treating or preventing the rejection of transplanted organs, tissues or cells by administering a pharmaceutical composition comprising the antagonist Met-RANTES and Cyclosporin, and a pharmaceutical composition comprising Met-RANTES and Cyclosporin, is not commensurate in scope with the claims drawn for a method of treating or preventing the rejection of transplanted organs, tissues or cells by administering a pharmaceutical composition comprising "all possible" RANTES receptor antagonists and Cyclosporin or a pharmaceutical composition comprising "all possible" RANTES receptor

antagonists and Cyclosporin, or wherein said RANTES receptor antagonist is amino-terminally truncated, or amino-terminally extended

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116).

Instant specification discloses that adding a single methionine at the N-terminus of RANTES changes the agonist protein into a RANTES receptor antagonist with nonmolar potency, and that treatment of rat renal transplant model with Met-RANTES in combination with low dose of Cyclosporin caused a significant reduction of interstitial rejection in renal allograft transplantation, (page 16). Thus the only amino-terminally extended RANTES receptor antagonist to be used in combination with Cyclosporin, disclosed by Applicants is Met-RANTES With the exception of Met-RANTES the skilled artisan cannot envision the detailed structure of other RANTES receptor antagonists encompassed by instant claims, therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of making it. With respect to claims 20, 21, 27, 31, 32 and 37 Applicants do not provide any guidance as to how many amino acids to delete from the N-terminus or how many amino acids to add to the N-terminus of RANTES.

Furthermore, In *The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

Therefore, the written description in this case is only commensurate with Met-RANTES antagonist in combination with low dose of Cyclosporin to be used in the claimed method, and a pharmaceutical composition comprising the antagonist Met-RANTES and Cyclosporin.

Claims 22, 25, 33 and 36 are rejected under 35 U.S.C. 112, first paragraph, insofar as they depend on claim 17 and 30 for the limitations set forth directly above.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 17-22, 24-27, 29, 31 and 37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

4a. Claim 17 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The

omitted steps are: the claim is drawn to a method of treating or preventing the rejection of transplanted organs, tissues or cells by administering an antagonist and Cyclosporin, however the claim lacks a result step, i.e, what are the effects of the antagonist and Cyclosporin? Also "RANTES" is misspelled in the claim. Appropriate correction is required.

4b. Claims 20, 27, 31 and 37 recite ".... a truncated RANTES", however, it is unclear which portion of RANTES should be cleaved. Appropriate correction is requires.

Claims 18-19, 21-22, 24-26, 29 are rejected under 35 U.S.C. 112, second paragraph, insofar as they depend on claim 17 for the limitations set forth directly above.

Conclusion

5. No claim is allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fozia Hamud whose telephone number is (703) 308-8891. The examiner can normally be reached on Monday, Wednesday-Thursday from 6:30AM to 4:00PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4227. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Fozia Hamud
Patent Examiner
Art Unit 1647
12 March 2003

YVONNE EYLER, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600